Pregnant Women and Novel Influenza A (H1N1) Virus: Considerations for Clinicians

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This document provides updated, interim guidance on the use of influenza antiviral treatment of pregnant women who are sick with novel influenza A (H1N1). The highest priority message is to treat pregnant women with influenza-like illness as soon as possible; treatment should not be withheld pending results of testing for influenza, if testing is done. Influenza antiviral chemoprophylaxis recommendations have been updated to be consistent with CDC recommendations for chemoprophylaxis for high risk groups. Finally, infant feeding recommendations have been updated to reflect current mask use guidance and the need for a cautious approach to preventing infection in infants, even though clinical data are lacking. Recommendations are interim, based on current knowledge of the H1N1 outbreak in the United States, and may be revised as more information becomes available.

Background

Human infections with a novel influenza A (H1N1) virus that is easily transmissible among humans were first identified in April 2009. Severe illnesses among pregnant woman and infants have been reported in this outbreak (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5818a3.htm) although the epidemiology and spectrum of illness among pregnant woman and infants are not fully understood at this time and are under investigation.

However, evidence that influenza can be more severe in pregnant women is available from observations during previous pandemics and from studies among pregnant women who had seasonal influenza. An excess of influenza-associated deaths among pregnant women were reported during the pandemics of 1918–1919 and 1957–1958. Adverse pregnancy outcomes have been reported following previous influenza pandemics, with increased rates of spontaneous abortion and preterm birth reported, especially among women with pneumonia. Case reports and several epidemiologic studies conducted during interpandemic periods also indicate that pregnancy increases the risk for influenza complications for the mother and might increase the risk for adverse perinatal outcomes or delivery complications.

Clinical presentation

Pregnant women with novel influenza A (H1N1) virus infection would be expected to present with typical acute respiratory influenza-like illness (e.g., cough, sore throat, rhinorrhea) and fever. Other symptoms can include body aches, headache, fatigue, vomiting and diarrhea. Many pregnant women will go on to have a typical course of uncomplicated influenza. However, for some pregnant women, illness might progress rapidly, and might be complicated by secondary bacterial infections including pneumonia. Fetal distress associated with severe maternal illness can occur. Case reports of adverse pregnancy outcomes and maternal deaths have been associated with severe illness. Ideally, pregnant women who have suspected novel influenza A (H1N1) virus infection should be tested for influenza. However, treatment should not be delayed pending results of testing and treatment should not be withheld in the absence of testing. This is because antiviral treatment is most effective when started as early as possible after the onset of symptoms (i.e. within the first 2 days). Testing is not available in many instances and, when available, results of novel H1N1 testing often take several days. Clinicians should be aware of circulation of H1N1 in their area and not wait for test results to initiate influenza treatment in women who have symptoms consistent with influenza illness.

Treatment and chemoprophylaxis

Early treatment with influenza antiviral medications is recommended for pregnant women with suspected influenza illness. Clinicians should not wait for test results to initiate treatment since these medications work best if started as early as possible after illness onset. The currently circulating novel influenza A (H1N1) virus is sensitive to the neuraminidase inhibitor antiviral medications zanamivir (Relenza®) and oseltamivir (Tamiflu®), but is resistant to the adamantane antiviral medications, amantadine (Symmetrel®) and rimantadine (Flumadine®). Oseltamivir is given orally and results in systemic absorption; by contrast, zanamivir is given by inhalation and results in lower systemic absorption. Oseltamivir and zanamivir treatment and chemoprophylaxis regimens recommended for pregnant women are the same as those recommended for adults who have seasonal influenza. Pregnancy should not be considered a contraindication to oseltamivir or zanamivir use.

Pregnant women appear to be at higher risk for severe complications from novel influenza A (H1N1) virus infection, and the benefits of treatment or chemoprophylaxis with oseltamivir or zanamivir outweigh the theoretical risks of antiviral use. Although a few adverse effects have been reported in pregnant women who took these medications, no relation between the use of these medications and those adverse events has been established. More information on influenza antiviral medications is available at: CDC Interim Guidance on Antiviral Recommendations for Patients with Novel Influenza A (H1N1) Virus Infection and Their Close Contacts (http://www.cdc.gov/h1n1flu/recommendations.htm) .

Treatment Recommendations

Pregnant women with influenza-like illnesses should receive empiric antiviral treatment. Because of its systemic activity, the drug of choice for treatment of pregnant women is oseltamivir. Recommended duration of treatment is five days. Treatment should not be delayed while waiting for the results of viral testing. As is recommended for other persons who are treated, antiviral treatment should be initiated as soon as possible after the onset of influenza symptoms, with benefits expected to be greatest if started within 48 hours of onset, based on data from studies of seasonal influenza. However, data from studies on seasonal influenza indicate benefit for hospitalized patients even if treatment is started more than 48 hours after onset. Thus, antiviral medications are recommended for high risk persons, including pregnant women, presenting for care more than 48 hours after illness onset, particularly for those who require hospitalization

Chemoprophylaxis Recommendations

Post exposure antiviral chemoprophylaxis can be considered for pregnant women who are close contacts of persons with suspected or laboratory confirmed novel influenza A (H1N1) virus infection. The drug of choice for prophylaxis is probably zanamivir because of its limited systemic absorption. However, respiratory complications that may be associated with zanamivir because of its inhaled route of administration need to be considered, especially in women at risk for respiratory problems. For these women, oseltamivir is a reasonable alternative. Recommended duration of chemoprophylaxis is for 10 days after the last known exposure to novel influenza A (H1N1). In situations where multiple exposures are likely to occur, such as within families, the total length of chemoprophylaxis for a pregnant woman may depend on clinical considerations. Close monitoring for influenza like illness in exposed pregnant women is recommended.

Fever Treatment

One of the more well-studied adverse effects of influenza is its associated hyperthermia. Studies have shown that maternal hyperthermia during the first trimester doubles the risk of neural tube defects and may be associated with other birth defects and adverse outcomes. Limited data suggest that the risk for birth defects associated with fever might be mitigated by antipyretic medications and/or multivitamins that contain folic acid. Maternal fever during labor has been shown to be a risk factor for adverse neonatal and developmental outcomes, including neonatal seizures, encephalopathy, cerebral palsy, and neonatal death. Even though distinguishing the effects of the cause of fever from the hyperthermia itself is difficult, fever in pregnant women should be treated because of the risk that hyperthermia appears to pose to the fetus. Acetaminophen appears to be the best option for treatment of fever during pregnancy.

Table 1 below is extracted from the guidance on influenza antiviral medications. Additional information on influenza antiviral medications can be found at recommendations (http://www.cdc.gov/h1n1flu/recommendations.htm) .

Table 1. Antiviral medication dosing recommendations for treatment or chemoprophylaxis of novel influenza A (H1N1) infection
(Table extracted from IDSA guidelines for seasonal influenza (http://www.journals.uchicago.edu/doi/full/10.1086/598513) .)

Agent, group	Treatment	Chemoprophylaxis
Oseltamivir		
Adults	75-mg capsule twice per day for 5 days	75-mg capsule once per day
Zanamivir		
Adults	Two 5-mg inhalations (10 mg total) twice per day for 5 days	Two 5-mg inhalations (10 mg total) once per day

Other ways to reduce risk for pregnant women

There is no vaccine available yet to prevent novel influenza A (H1N1) virus infection; however, the risk for novel influenza A (H1N1) virus infection might be reduced by taking steps to reduce the chance of being exposed to respiratory infections. These steps include:

1. Frequent hand washing.
2. Minimizing contact with sick individuals.
3. Having ill persons stay home (except to seek medical care).
4. Having ill persons cover coughs.
5. Avoiding, whenever possible, crowded settings in communities having outbreaks of novel influenza A (H1N1) virus.
6. And using facemasks and respirators correctly if they are used (see Interim Recommendations for Facemask and Respirator Use to Reduce Novel Influenza A (H1N1) Virus Transmission (http://www.cdc.gov/h1n1flu/masks.htm)).

Infant feeding considerations

Infants who are not breastfeeding are more vulnerable to infection and hospitalization for severe respiratory illness than infants who are breastfeeding. Women who are not ill with influenza should be encouraged to initiate breastfeeding early and feed frequently. Ideally, babies should receive most of their nutrition from breast milk. Eliminate unnecessary formula supplementation, so the infant can receive as much maternal antibodies as possible

Infants are thought to be at higher risk for severe illness from novel influenza A (H1N1) infection and very little is known about prevention of novel H1N1 flu infection in infants. If possible, only adults who are not sick should care for infants, including providing feedings. The risk for novel influenza A (H1N1) transmission through breast milk is unknown. However, reports of viremia with seasonal influenza infection are rare, which suggests that the risk of virus crossing into breast milk is also probably rare. Sick women who are able to express their milk for bottle feedings by a healthy family member should be encouraged to do so. Antiviral medication treatment or prophylaxis is not a contraindication for breastfeeding.

Careful adherence to hand hygiene and cough etiquette is critical, especially for sick women who do not have anyone to help with infant care while they are ill. Women with influenza-like illness are recommended to use facemasks when providing infant care and feedings (see Interim Recommendations for Facemask and Respirator Use to Reduce Novel Influenza A (H1N1) Virus Transmission (http://www.cdc.gov/h1n1flu/masks.htm)).

Instruct parent and caretakers on how to protect their infant from the spread of germs, like novel influenza A (H1N1) virus, that cause respiratory illnesses:

- Practice hand hygiene and cough etiquette (http://www.cdc.gov/h1n1flu/qa.htm) at all times
- Keep the infant away from persons who are ill and out of crowded areas.
- Limit sharing of toys and other items that have been in infants' mouths. Wash thoroughly with soap and water any items that have been in infants' mouths.

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